Original Article

# Pulmonary Hypertension in Posttubercular Pulmonary Fibrosis: A Prospective Study from Western Himalayas

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## Abstract

**Introduction:** Pulmonary tuberculosis (PTB) has been linked to a high rate of morbidity and mortality. Studies that assessed the impact of treated PTB as a cause of disability have focused on impairment of pulmonary function. Pulmonary hypertension (PH) must be assessed in patients with posttubercular pulmonary fibrosis. The goal of this study was to use Doppler echocardiography to determine the prevalence of PH in individuals with posttubercular pulmonary fibrosis. **Materials and Methods:** It was a prospective cross-sectional hospital-based study carried out over a period of 1 year. Patients having posttubercular pulmonary fibrosis were enrolled after fulfilling the inclusion and exclusion criteria, further evaluated by Doppler echocardiography for PH. **Results:** A total of 80 patients with the most common age group of 31–40 years and female predominance were involved in the study. Dyspnea was the most common symptom being reported by 100% of the patients, followed by cough (32.5%), hemoptysis (22.5%), chest pain (10%), and syncope (2.5%). Tricuspid regurgitation velocity was found <2.8 m/s in 52.5%, between 2.9 and 3.4 m/s in 30% and >3.4 m/s in 17.5% patients. In our study, mild PH was present in 25%, moderate PH in 6.3%, and severe PH in 16.3% of patients with an insignificant $P = 0.200$. **Conclusions:** Tuberculosis may have a causal association with PH. The results of the present study suggest that 2D echocardiography is a useful tool in diagnosing pulmonary hypertension in posttubercular pulmonary fibrosis.

**Keywords:** Echocardiography, fibrosis, hypertension, posttubercular, pulmonary

## Introduction

Mycobacterium tuberculosis, discovered by Robert Koch in 1882, is one of the leading causes of death in humans. Tuberculosis is the world's ninth leading cause of mortality and the leading cause of death caused by a single infectious agent. Despite modern and efficient chemotherapy, pulmonary tuberculosis (PTB) continues to cause significant morbidity and mortality.[1] Treatment success in PTB has been defined in terms of microbiological culture rates and little attention has been paid to the impact of PTB as a cause of disability in those who survived the disease.

Given the high occurrence of PTB and the excellent success rate of the current therapy, an unknown but significant number of patients worldwide have survived PTB. The impairment of pulmonary function has been the subject of studies evaluating the impact of treated PTB as a cause of disability. In more than half of the treated PTB patients, these investigations found considerable residual lung function impairment, with both obstructive and restrictive ventilatory abnormalities identified.[2,3] Persistent physiological impairment is known to produce gas exchange irregularities and the development of pulmonary hypertension (PH), which causes severe disability and shortens life expectancy.[4-6]

PH can be caused by a variety of respiratory and nonrespiratory factors (PH). Chronic obstructive pulmonary disease (COPD), idiopathic pulmonary fibrosis, obstructive sleep apnea, and PTB are the most common respiratory disorders that cause PH. The prevalence of PH in various respiratory disorders has been investigated in several noninvasive and invasive research.[4,7-10]

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Patients with posttubercular pulmonary fibrosis must be evaluated for PH using a multimodality approach, which includes a series of investigations ranging from a thorough clinical evaluation, noninvasive imaging, and right heart catheterization (RHC), which is considered the "gold standard" for the diagnosis of PH.[11,12]

Transthoracic echocardiography provides several measures that can be used to estimate right heart hemodynamics like pulmonary artery systolic pressure (PASP) calculated from the tricuspid regurgitant velocity (TRV) and is used to alert suspicion of PH. The estimation of PASP is based on the peak TRV taking into account the right atrial pressure (RAP) as described by the simplified Bernoulli equation.[13,14] The goal of this study was to use Doppler echocardiography to determine the prevalence of PH in patients with posttubercular pulmonary fibrosis.

## Materials and Methods

It was a prospective cross-sectional hospital-based study conducted in the Department of Pulmonary Medicine and Cardiology from July 2016 to June 2017. After receiving approval from the institutional ethical committee, all consecutive patients with posttubercular pulmonary fibrosis were enrolled in the study. Written informed consent was taken from all patients who met the inclusion criteria (radiological characteristics of pulmonary fibrosis after tuberculosis with age <40 years) and the exclusion criteria, i.e., age >40 years (because COPD occurs predominantly in the age group of more than 40 years, which is one of the major causes of PH), HIV-positive patients, COPD patients, Cardiac disease (valvular or myocardial disease), pulmonary fibrosis other than tuberculosis, pulmonary thromboembolism, and poor echocardiography window.

Doppler echocardiography was used to check for PH in patients with pulmonary fibrosis. Doppler echocardiography was used to do a thorough cardiac assessment, and PH was established by measuring the PASP. Echocardiography was performed utilizing a Philips medical system iE33 echo machine with a 2–5 broadband phased array probe to record various parameters.

The effects of PH on the heart were imaged using transthoracic echocardiography, and PASP was estimated using continuous-wave Doppler measurements. All measurements were done as per the standard echocardiographic guidelines. PH was graded based on PASP, i.e., normal (<40 mmHg), mild (41–50 mmHg), moderate (51–80 mmHg), and severe (>80 mmHg).

The peak tricuspid regurgitation velocity (TRV) was used in conjunction with the presence of other echo PH symptoms to determine the probability of PH. The patients were separated into three groups based on their PH risk: low, middle, and high. Low PH-risk was defined as TRV 2.9 m/s (or not measurable) with no more than one additional echocardiography PH sign; intermediate risk was defined as TRV 2.9 m/s with two additional PH signs, or TRV 2.9–3.4 m/s with no more than one additional PH sign; high risk was defined as TRV 2.9–3.4 m/s with two additional PH signs, or TRV >3.4 m/s with two additional PH.

In addition to the PASP and routine echocardiographic findings, the following parameters were noted: pulmonary artery acceleration time and inferior vena cava (IVC) diameter with response to inspiration. An echocardiographic scan will be performed to rule out any left atrial or left ventricle illness that could be causing PH.

The information was entered into a Microsoft Excel spreadsheet. Tables and percentages were used to summarize the findings. The statistical SPSS program version 22 (IBM, Chicago IL, USA) was used to do cross-tabulation with the outcome variable of interest. Statistical significance was defined as a $P < 0.05$. Standard statistical procedures were used to calculate the test's sensitivity, specificity, positive predictive value, and negative predictive value.

## Results

A total of 80 patients were involved in the study of different age groups. The most common age group involved in the study was 31–40 years (65%) [Table 1]. The youngest patient was aged 18 years and the oldest one was 40 years. In this study, 45 (56.2%) were female and 35 (43.8%) were male.

The analysis of symptoms among the patients revealed dyspnea as the most common symptom being reported by 80 patients (100%), followed by cough in 26 (32.5%), hemoptysis in 18 (22.5%), chest pain in 8 (10%), and syncope in 2 (2.5%) patients. Grading of dyspnea was done according to the modified medical research council Scale. In this study, 39 patients (48.8%) have Grade I dyspnea, 17 (21.3%) had Grade II dyspnea, 10 (12.5%) had Grade 0 dyspnea, and 7 (8.8%) had Grade III and 7 (8.8%) has Grade IV dyspnea. After analysis of D-dimer and HIV, D–Dimer was found <0.5 mcg/ml in all 80 patients so pulmonary thromboembolism was ruled out on this basis and also on a clinical basis. HIV was also nonreactive in all the 80 patients.

In our study, TRV was found <2.8 m/s in 42 patients (52.5%), between 2.9 and 3.4 m/s in 24 patients (30.0%) and more than 3.4 m/s in 14 (17.5%) patients. In our study, TRV gradient was found <30 mmHg in 42 patients (52.5%) and >30 mmHg in 38 (47.5%) patients. In this study, 38 patients (47.5%) had low probability of PH, 18 patients (22.5%) had intermediate probability of PH and 24 patients (30%) had high probability of PH.

**Table 1: Distribution of study group by age ($n=80$)**

| Age group (years) | Number of patients, *n* (%) |
|---|---|
| <20 | 4 (5) |
| 21-30 | 24 (30) |
| 31-40 | 52 (65) |

In our study, PASP was found to be normal, i.e., is <40 mmHg in 42 patients (52.5%), mild PH i.e., PASP between 41 and 50 mmHg in 20 patients (25.0%), moderate PH, i.e., PASP between 51 and 80 mmHg in 5 patients (6.3%) and severe PH, i.e., PASP >80 mmHg in 13 (16.3%) patients [Table 2]. *P* value was insignificant (0.200).

In our study, the analysis of chest X-rays for the type of lesion revealed that 48 patients (60%) had fibrosis and 32 patients (40%) had fibrocavitary lesions. On chest X-ray, 21 patients (26.3%) had involvement of only one zone of the lung, 30 patients (37.5%) had involved two zones of the lung and 29 patients (36.3%) had involved three or more than three zones of lung. Out of 38 patients who had PH 31 patients (81.57%) had involved two or more two zones of the lung on chest X-ray.

In our study, pulmonary artery acceleration time <105 ms was found in 28 patients (35.0%) and >105 ms in 52 patients (65.0%). IVC collapses <50% was found in 19 patients (23.8%) and collapses >50% in 61 patients (76.3%). During echocardiography, tricuspid annular plane systolic excursion (TAPSE) <18 mm was found in 15 patients (18.7%) and TAPSE >18 mm was found in 65 patients (81.3%). In our study, none of the 80 patients had any disease of the left ventricle, mitral valve, and left atrium or any filling defect in the pulmonary artery.

## Discussion

PH as a result of primary pulmonary diseases usually heralds a poor prognosis. The association between active tuberculosis and PH has been assessed in a few previous studies, in which PH or cor pulmonale was diagnosed either by electrocardiography or during postmortem examination.[5,15,16]

In a cross-sectional study, Ahmed *et al*.[17] described 14 patients who presented with shortness of breath after successful treatment of PTB. PH was evaluated by Doppler echocardiography. The clinical profile and prevalence of PH in patients with posttubercular fibrosis by Doppler echocardiography were evaluated in our study.

The most common age group in the study was 31–40 years (65%). The youngest patient was aged 18 years and the oldest one was 40 years. Kapoor[16] reported the following age distribution in 66 patients with PTB; 3% of cases were of age <10 years, 16.66% of patients of age 11–20 years, 46.96% of patients of age 21–30 years, 10.6% of patients of age 31–40 years, 13.63% of patients of age 41–50 years and 9% of patients of age more than 50 years. The youngest patient was 6-year-old, and the oldest was 66 years. HIV test was done in all patients and found to be nonreactive in all patients. The difference in the age between the two studies may be because we excluded patients more than 40 years.

**Table 2: Pulmonary artery systolic pressure (*n*=80)**

| PASP (mmHg) | Number of patients, *n* (%) |
|---|---|
| <40 (normal) | 42 (52.5) |
| 41-50 (mild) | 20 (25) |
| 51-80 (moderate) | 5 (6.3) |
| >80 (severe) | 13 (16.3) |

PASP: Pulmonary artery systolic pressure

Females constituted the majority of our study population, i.e., 45 (56.2%) females and 35 (43.8%) males. Ahmed *et al*.[17] Observed 50% female and 50% male patients among the cohort of post-TB fibrosis patients. Similarly, Marjani *et al*.[18] reported 54.1% females and 45.9% males in their study and figures are comparable to our study.

In the present study, dyspnea was the most common symptom being reported by all 80 patients (100%), followed by cough in 26 (32.5%), hemoptysis in 18 (22.5%), chest pain in 8 (10%), and syncope in 2 (2.5%) patients. Studies in the literature[16,18,19] reported dyspnea in 59%–98% of patients. Patel *et al*.[19] reported cough in 92% of patients with PH. Such high incidence could be due to the inclusion of the patients with COPD, interstitial lung disease, bronchiectasis, tuberculosis, bronchial asthma, and kyphoscoliosis in their study while we included only patients with posttubercular fibrosis in our study.

In our study, the analysis of chest X-rays for the type of lesion revealed that 48 patients (60%) had fibrosis and 32 patients (40%) had fibrocavitary lesions. Ahmed *et al*.[17] reported that 57% of patients had fibrocavitary lesions, 36% had fibrosis, 7% had both bullae and fibrosis, and 7% had fibrothorax on chest X-ray. Kapoor[16] reported giant cavities in 31.8% of patients and diffuse fibrosis in 36.36% of patients on chest X-rays in the study.

In this study, 21 patients (26.3%) had involvement of only one zone of the lung, 30 patients (37.5%) had involved two zones of the lung, and 29 patients (36.3%) had involved three or more than three zones of the lung. Kapoor[16] reported that 36.36% of patients had involvement of <1 lobe of the lung, 40.9% had involvement of more than one lobe of the lung but <1 lung field unit, and 22.72% had more than one lung field involved in their study. Hence, figures are comparable to our study.

In our study, TRV was found <2.8 m/s in 42 patients (52.5%), between 2.9 and 3.4 m/s in 24 patients (30.0%) and more than 3.4 m/s in 14 (17.5%) patients. In our study, TRV gradient was found <30 mmHg in 42 patients (52.5%) and >30 mmHg in 38 (47.5%) patients. PH was found among 38 patients, 20 patients (25%) had mild PH, 5 patients (6.3%) had moderate PH and 13 patients (16.3%) had severe PH. Ahmed *et al*.[17] reported mild PH in 4 patients (28.6%), moderate–severe PH in 9 patients (64.3%), and severe PH in one patient (7.1%). Marjani *et al*.[18] reported systolic pulmonary arterial pressure >35 mm Hg in 9.5% of patients. The difference between our study and these studies may be because of the fact that these studies included the patients with active tuberculosis also so there may not be enough

destruction of the lungs to cause hypoxia and PH. Hence, it indicates that there are also other factors such as duration of disease and extent of parenchymal destruction which determine the prevalence of PH.

Residual lung structural damage and pulmonary function abnormalities, which contribute to gas exchange abnormalities and chronic hypoxia, are thought to be the cause of PH in treated pulmonary TB patients. Repeated secondary respiratory tract infections, produced by residual chest X-ray abnormalities, have also been postulated to have a role in the etiology of PH in individuals with PTB. All our patients had abnormal chest radiographs that were caused by pulmonary TB, but we did not measure lung function in our study population.

The small sample size used in this study is a methodological flaw, and higher sample size is advised for future research. Measurement of PASP by echocardiography in patients with severe tricuspid regurgitation may lead to underestimation. Furthermore, overestimation is common. As a result, echocardiography may not be a good screening tool for asymptomatic mild PH patients. Although our research demonstrates the importance of PH in posttubercular fibrosis, many questions remain unanswered, such as what are the risk factors for PH in posttubercular fibrosis? Is PH screening recommended for every case of posttubercular fibrosis, or at the very least for those who are at high risk for PH? What is the best tool for this type of screening? After detection of PH, is there any intervention that could improve the outcome of TB patients? Prospective well-designed studies are necessary to respond to these questions.

## Conclusions

India is one of the countries with a high prevalence of PTB, and early detection is critical due to posttubercular complications. The "Tuberculosis-associated PH" as reported by us appears to be a separate entity based on our observations. Tuberculosis may be linked to PH, and a history of PTB should be sought in all patients of PH, particularly in developing countries. The findings of this study indicate that 2D echocardiography can be used to diagnose PH in patients with posttubercular pulmonary fibrosis. Although RHC is the gold standard and required for PH confirmation, it is an intrusive and expensive treatment that is inappropriate for use as a screening tool. The use of transthoracic Doppler echocardiography to screen for PH has been proved to be a safe, sensitive, and specific approach.

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### Conflicts of interest

There are no conflicts of interest.

## References

1. WHO. Global Tuberculosis Report 2017. Licence: CC BY-NCSA 3.0 IGO. Geneva, Switzerland: World Health Organization; 2017.
2. Snider GL, Doctor L, Demas TA, Shaw AR. Obstructive airway disease in patients with treated pulmonary tuberculosis. Am Rev Respir Dis 1971;103:625-40.
3. Birath G, Caro J, Malmberg R, Simonsson BG. Airways obstruction in pulmonary tuberculosis. Scand J Respir Dis 1966;47:27-36.
4. Pasipanodya JG, Miller TL, Vecino M, Munguia G, Garmon R, Bae S, *et al*. Pulmonary impairment after tuberculosis. Chest 2007;131:1817-24.
5. Seeger W, Adir Y, Barberà JA, Champion H, Coghlan JG, Cottin V, *et al.* Pulmonary hypertension in chronic lung diseases. J Am Coll Cardiol 2013;62 25 Suppl: D109-16.
6. Simpson DG, Uschner M, Mc Clement J. Respiratory function in pulmonary tuberculosis. Am Rev Respir Dis 1963;87:1-16.
7. Shorr AF, Wainright JL, Cors CS, Lettieri CJ, Nathan SD. Pulmonary hypertension in patients with pulmonary fibrosis awaiting lung transplant. Eur Respir J 2007;30:715-21.
8. Nathan SD, Shlobin OA, Weir N, Ahmad S, Kaldjob JM, Battle E, *et al*. Long-term course and prognosis of idiopathic pulmonary fibrosis in the new millennium. Chest 2011;140:221-9.
9. Rivera-Lebron BN, Forfia PR, Kreider M, Lee JC, Holmes JH, Kawut SM. Echocardiographic and hemodynamic predictors of mortality in idiopathic pulmonary fibrosis. Chest 2013;144:564-70.
10. Naeije R. Pulmonary hypertension and right heart failure in chronic obstructive pulmonary disease. Proc Am Thorac Soc 2005;2:20-2.
11. Zisman DA, Karlamangla AS, Ross DJ, Keane MP, Belperio JA, Saggar R, *et al*. High-resolution chest CT findings do not predict the presence of pulmonary hypertension in advanced idiopathic pulmonary fibrosis. Chest 2007;132:773-9.
12. Patel NM, Lederer DJ, Borczuk AC, Kawut SM. Pulmonary hypertension in idiopathic pulmonary fibrosis. Chest 2007;132:998-1006.
13. Vakil RJ. Cardiovascular diseases in India. Am J Cardiol 1962;10:380-9.
14. Janda S, Shahidi N, Gin K, Swiston J. Diagnostic accuracy of echocardiography for pulmonary hypertension: A systematic review and meta-analysis. Heart 2011;97:612-22.
15. Arcasoy SM, Christie JD, Ferrari VA, Sutton MS, Zisman DA, Blumenthal NP, *et al*. Echocardiographic assessment of pulmonary hypertension in patients with advanced lung disease. Am J Respir Crit Care Med 2003;167:735-40.
16. Kapoor SC. Pathogenesis of cor pulmonale in pulmonary tuberculosis. Indian J Tuberc 1986;33:167-70.
17. Ahmed AE, Ibrahim AS, Elshafie SM. Pulmonary hypertension in patients with treated pulmonary tuberculosis: Analysis of 14 consecutive cases. Clin Med Insights Circ Respir Pulm Med 2011;5:1-5.
18. Marjani M, Baghaei P, Malekmohammad M, Tabarsi P, Sharif-Kashani B, Behzadnia N, *et al*. Effect of pulmonary hypertension on outcome of pulmonary tuberculosis. Braz J Infect Dis 2014;18:487-90.
19. Patel V, Khaped K, Solanki B, Patel A, Rathod H, Patel J. Profile of pulmonary hypertension patients coming to Civil Hospital, Ahmedabad. Int J Res Med 2013;2:94-7.